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About Osteoporosi

Osteoporosis is a disease characterized by low bone mass and structural deterioration of bone tissue, leading to bone fragility and an increased susceptibility to fractures -- especially of the hip, spine, and wrist. It is the most prevalent of the bone diseases that affect Americans. Although it is the underlying cause of most fractures in older people, the condition is silent and undetected in most cases until a fracture occurs.

Osteoporosis is a major threat for 28 million Americans. In the U.S. today, 10 million individuals already have osteoporosis and 18 million more have low bone mass, placing them at increased risk for this disease. American women are four times as likely to develop osteoporosis as men. One out of every two women and one in eight men over 50 will have an osteoporosis-related fracture in his or her lifetime.

Osteoporosis is responsible for more than 1.5 million fractures annually, including 300,000 hip fractures, approximately 700,000 vertebral fractures, 200,000 wrist fractures, and more than 300,000 fractures at other sites.

Of all these injuries, hip fractures have the greatest morbidity and socioeconomic impact. Following a hip fracture, there is a 10 to 20 percent mortality rate during the next 6 months. This means people can, and do, die as a result of hip fractures. Fifty percent of those people experiencing a hip fracture will be unable to walk without assistance, and 25 percent will require long-term care. The burden of health care costs due to osteoporotic fractures is estimated to be approximately $14 billion per year.

Osteoporosis, however, does not need to be a consequence of aging. It is largely a preventable disease, and many research opportunities exist to enhance our knowledge about how to maintain a healthy skeleton throughout life.

Remarkable progress has been made in our understanding of the causes, diagnosis, treatment, prevention of osteoporosis. However, many avenues of scientific opportunity remain. Every increment of research progress brings us closer to eliminating the pain and suffering caused by this disease.

Addressing Osteoporosis: A Collaborative Approach

Significant efforts are underway at the Federal level aimed at addressing this serious public health problem. In particular, several components of the National Institutes of Health (NIH) are currently supporting basic and/or clinical research on osteoporosis and related bone diseases. The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) has taken the lead in initiating the Federal Working Group on Bone Diseases. Launched in 1993, this group provides a forum for the sharing of information between NIH institutes and other Federal agencies to enhance communication and to coordinate research efforts across all Federal agencies with an interest in bone diseases and bone health.

The Study of Osteoporotic Fractures (SOF), supported by NIAMS and the National Institute on Aging (NIA), and involving more than 9,000 women 65 years or older, described risk factors for hip, wrist, and

spine fractures. The study demonstrated that bone mineral density predicts hip and other types of fractures, and also provided evidence that women with low bone density have an increased risk of stroke, as well as evidence of a relationship between bone mineral density and breast cancer incidence. The NIH Women's Health Initiative currently supports the largest study of osteoporosis and fractures ever conducted. This study will determine the usefulness of calcium and vitamin D supplements, and may lead to new public health initiatives to optimize the intake of these nutrients in the U.S. population.

Addressing Osteoporosis: NIAMS' Research Agenda

NIAMS leads the Federal research effort on osteoporosis and related bone diseases, and is responsible for nearly half of the NIH funding for research in this area (which totaled over $120 million in FY 1998). NIAMS-supported research ranges from very basic studies to clinical and translational research and early intervention and prevention projects, such as "Camp Calcium," a novel program for adolescent girls, which has as its goal the determination of how much calcium growing girls need in their diets so that they can develop the strongest possible bones, and thus help reduce their chance of getting osteoporosis later in life.

Overall, significant advances in prevention and treatment of osteoporosis are available today as the direct result of research focused on determining the causes and consequences of bone loss at cellular and tissue levels, assessing risk factors, developing strategies to maintain and even enhance bone density, and exploring the roles of such factors as hormones, calcium, vitamin D, drugs, and exercise on bone mass.

Selected Scientific Advances

A number of recent advances illustrate the progress being made in understanding osteoporosis and how it might be treated and prevented:

The finding that low-dose hormone replacement therapy (HRT) prevents bone loss -- A study published just this month has revealed that women well past menopause can profitably take a lower dose of estrogen than is commonly prescribed, in combination with a sufficient intake of vitamin D and calcium supplements, and achieve gains in bone mass without the negative side effects associated with higher doses of estrogen. This is especially significant as estrogen replacement is now the cornerstone of osteoporosis treatment and prevention.

Findings on steroid-induced bone loss in mice point to preventive possibilities -- Investigators have recently used a mouse model and cell culture techniques to shed light not only on the destructive mechanism of glucocorticoids -- a class of steroidal immunosuppressive medications -- but also on ways to prevent steroid-induced bone loss. Steroid-induced osteoporosis is common among transplant patients, as well as those who suffer from chronic autoimmune diseases, such as lupus and rheumatoid arthritis.

The identification of a gene essential for the formation of bone -- Through a convergence of efforts by investigators around the world, research has shown that normal skeletal development -in both mice and humans -- apparently requires two active copies of the gene Cbfal. This discovery is expected to open a number of exciting new research areas.

The finding that estrogen induces "programmed cell death" in the cells that are responsible for the degradation of bone (osteoclasts) -- By paving the way for future assessment of whether other drugs can also affect the programmed cell death of osteoclasts (thereby making them potentially useful as bone-

protecting treatments), this discovery represents an exciting link between basic research and tangible patient benefit.

The finding that one of a collection of molecules fabricated by researchers (called peptidomimetics successfully blocks part of the bone resorption process -- This is the first clear indication that a particular synthetic antagonist may be effective in the prevention of osteoporosis. The finding may hold promise for combating bone loss in women who cannot tolerate estrogen.

Patient-based research showing that elderly women who already had several spine fractures at the start of a study experienced the greatest health benefit from calcium supplementation (both in terms of reduction in the rate of new spine fractures and cessation of bone loss) -- This finding has clear implications for developing and targeting new preventive strategies.

Current and Planned Initiatives

In the past decade, there has been an explosion of basic and clinical research in osteoporosis. Many fundamental advances in molecular and cellular biology, immunology, genetics, and bioengineering could be applicable to skeletal biology. In addition, research on a new class of drugs called Selective Estrogen Receptor Modulators (SERM's) also holds promise in terms of reducing bone loss in postmenopausal women without adverse effects on other organs.

Alendronate, a bisphosphonate, was recently approved by the Food and Drug Administration for treatment of postmenopausal osteoporosis. This class of drugs targets bone specifically, reducing bone breakdown and decreasing fractures in older women. This development, along with other advances, creates vast opportunities to expand the current knowledge base, continuing in a diversified approach to osteoporosis. Initiatives which may serve as a springboard for further research include:

Multi-center clinical intervention studies on combination therapies for osteoporosis -- Because pharmaceutical companies tend to focus resources on bringing individual drugs to market, Federal support is needed to test combinations of drugs, as well as possible exercise and nutritional modifications to various drug combination regimes. Lower doses combinations of effective agents may serve to reduce side effects and risks associated with current individual drug treatments, and may improve overall responsiveness. These studies will also generate information on osteoporosis in men, children, adolescents, and others who have diseases and conditions that put them at high risk of osteoporosis, not just on postmenopausal women, the group on whom most private sector research has been concentrated. To this end, the NIAMS recently issued a request for proposals to uncover which combination therapies for osteoporosis optimize improvements in bone mass and bone strength while minimizing deleterious side effects.

Large epidemiologic study of osteoporosis in men to study risk factors for fracture development -- Although 50-year-old white men have about a 13 percent lifetime risk of fractures of the hip, spine, or wrist, the causes of and mechanisms involved in osteoporosis in men have received little research attention. Men develop osteoporosis and osteoporotic fractures about a decade later than women do. This has been attributed to a higher peak bone mass at maturity and a more gradual diminition in sex steroid influence in aging men. At each age the rate of hip fracture in men is about 50 percent that in women. With the decline in premature cardiovascular mortality in men, fractures later in life are becoming an increasingly important cause of morbidity and mortality in older men. NIAMS solicited research on the basic biology, epidemiology, prevention, and treatment of osteoporosis and osteoporosis-related fractures in men in order to reduce the incidence. In response to this solicitation, a large epidemiologic study will be launched to study the risk factors for fractures in men over age 65.

Development of new technologies to measure bone quality as well as bone mineral density --The need to evaluate the contribution of bone architecture -- in addition to bone mass -- in determining resistance of bone to fracture in vivo is spurring interest in new methods, which may include variations of micro-computed tomography or magnetic resonance imaging (MRI) techniques. Ultrasound technology is emerging as an alternative to bone densitometry for some clinical applications, and studies are also underway to develop blood and urine tests that may one day be used to screen for osteoporosis.

The Bone Density, Biomarkers and Physical Activity component of the National Health and Nutrition Examination Survey (NHANES) IV -- National Health and Nutrition Examination Surveys have been conducted periodically since the 1960's, via household interviews and physical examinations provided in specially designed mobile examination centers, and with data collections periods ranging from 3 to 6 years. NHANES IV is planned as a continuous survey with data collection beginning this year. NIAMS is specifically interested in information from three tests to be included in the exam: dual energy x-ray absorptiometry (DXA), measurements of markers of bone resorption in urine and blood samples, and assessment of musculoskeletal strength in participants aged 50 and over (one of two levels of physical fitness included for the first time in the Survey).

Research on bone and hematopoiesis (a process in which blood cells are produced, including the many different cells of the immune system) -- Following an August 1997 workshop, a program announcement has been developed which focuses on the interactions between two cellular systems which develop in close proximity in the bone marrow: the cells of the skeletal system (the cells that form and break down bone) and the cellular components of the immune system. The initiative will encourage collaboration between investigators with expertise in one area, such as bone biology or immunology, with other investigators having complementary expertise.

Research on riskfactorsfor bone fragility fractures in children and adolescents -- Current research is underway which will examine bone mineral density and measure dietary calcium intake in children and adolescents with distal forearm fractures and in normal controls. It is expected that this research will provide significant evidence that calcium may immediately reduce the number of fractures in children, and that it may serve to provide an incentive to families and their adolescent children to increase calcium intakes.

Consensus Development Conference on 0steoporosis Prevention, Diagnosis, and Therapy -- The last Consensus Development Conference on Osteoporosis (1984) marked a turning point in the view of the public and the research community about osteoporosis. Because there has been an explosion of information about diagnosis, treatment, and prevention since that time, an assessment of recent developments and research directions is warranted, aimed at ensuring that all physicians who see people at risk of osteoporosis -- not just expert bone endocrinologists -have the latest information. Accordingly, the NIAMS is sponsoring another osteoporosis consensus conference in March of 2000.

Information Dissemination and Education Efforts

The NIH Osteoporosis and Related Bone Diseases-National Resource Center was created by NIAMS in 1994 in response to a groundswell of interest by several voluntary and professional groups and key congressional leaders. Other Federal partners now support the Resource Center in addition to NIAMS, including NIA, as well as the National Institute of Child Health and Human Development, the National Institute of Dental and Craniofacial Research, the National Institute of Environmental Health Sciences, the NIH Office of Research on Women's Health and the HHS Office of Women's Health -- in cooperation with the National Osteoporosis Foundation, the Paget Foundation, and the Osteogenesis

Imperfecta Foundation. This Center provides an important link to resources and information on metabolic bone diseases, and its mission is to expand awareness and enhance knowledge and understanding of the prevention, early detection, and treatment of these diseases, as well as strategies for coping with them.

Through the Resource Center, collaborative efforts to enhance the strategies to promote bone health for women are being instigated through the National Osteoporosis Education Campaign. The initial focus of the campaign will be to encourage teenage women to develop positive health behaviors (for example, diet, exercise, calcium intake) that can have effects on bone strength that last a lifetime.

FEDERAL WORKING GROUP ON BONE DISEASES

Federal Member Organizations

National Institutes of Health:

National Institute of Arthritis and Musculoskeletal and Skin Diseases
National Institute of Child Health and Human Development
National Institute of Environmental Health Sciences
National Institute of Diabetes and Digestive and Kidney Diseases
National Cancer Institute
National Institute of Dental and Craniofacial Research
National Institute on Aging
National Institute of Nursing Research
National Institute on Alcohol Abuse and Alcoholism
National Center for Research Resources
Office of Research on Women's Health

Other Federal Agencies:

Agency for Health Care Policy and Research/Forum for Quality and Effectiveness of Health Care
Health Care Financing Administration/Office of Research and Demonstration
Department of Agriculture/Human Nutrition Research Center
Department of Defense/Army Operational Research Program
Centers for Disease Control and Prevention
National Center for Chronic Disease Prevention and Health Promotion
National Center for Health Statistics
Food and Drug Administration/Division of Metabolism and Endocrine Drug Products
Department of Education/National Institute on Disability and Rehabilitation Research
National Aeronautics and Space Administration/Life and Biomedical Sciences Applications Division

Liaison Organizations Federal and Non-Federal

NIH Office of Disease Prevention
NIH Clinical Center Nursing Department
NIH Nutrition Coordinating Committee
Department of Health and Human Services
Office on Women's Health
Administration on Aging
NIH Osteoporosis and Related Bone Diseases-National Resource Center
National Osteoporosis Foundation

The Paget Foundation
American Society for Bone and Mineral Research